CLAIMS

1. A replication-defective adeno-associated virus (AAV) comprising a correction genome enclosed in a capsid, wherein the capsid comprises an AAV Clade F capsid; and wherein the correction genome comprises:

(a) an editing element comprising an internucleotide bond or a nucleotide sequence for integration into a target locus of a mammalian chromosome;

(b) a 5' homologous arm nucleotide sequence 5' of the editing element, having homology to a 5' region of the mammalian chromosome relative to the target locus; and

(c) a 3' homologous arm nucleotide sequence 3' of the editing element, having homology to a 3' region of the mammalian chromosome relative to the target locus,

wherein the AAV Clade F capsid comprises an AAV capsid protein comprising:

(d) an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 203-736 of SEQ ID NO: 2, 3, 4, 6, 7, 10, 11, 12, 13, 15, 16, or 17, wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H;

the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A;

the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N;

the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S; the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y;

the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;

the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or

the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; and/or

(ii) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(e) an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 138-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, or 17, wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 151 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 160 of SEQ ID NO: 2 is D;

the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H;

the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A;

the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N;

the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S;

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y;

the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;

the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or

the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; and/or

(ii) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(f) an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 1-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, or 17, wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 2 of SEQ ID NO: 2 is T;

the amino acid in the capsid protein corresponding to amino acid 65 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 68 of SEQ ID NO: 2 is V;

the amino acid in the capsid protein corresponding to amino acid 77 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 119 of SEQ ID NO: 2 is L;

the amino acid in the capsid protein corresponding to amino acid 151 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 160 of SEQ ID NO: 2 is D;
the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C;
the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H;
the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;
the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A;
the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N;
the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S;
the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I;
the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R;
the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R;
the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y;
the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;
the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;
the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;
the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or
the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; and/or

(ii) the amino acid in the capsid protein corresponding to amino acid 2 of SEQ ID NO: 2 is T, and the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;
the amino acid in the capsid protein corresponding to amino acid 65 of SEQ ID NO: 2 is I, and the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is Y;
the amino acid in the capsid protein corresponding to amino acid 77 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;
the amino acid in the capsid protein corresponding to amino acid 119 of SEQ ID NO: 2 is L, and the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S;
the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;
the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;
the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;
the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or
the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C.

2. The AAV of claim 1, wherein the correction genome comprises a 5’ inverted terminal repeat (5’ ITR) nucleotide sequence 5’ of the 5’ homologous arm nucleotide sequence, and a 3’ inverted

terminal repeat (3' ITR) nucleotide sequence 3' of the 3' homologous arm nucleotide sequence, wherein:

(a) the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially identical to an AAV2 virus 5'ITR and an AAV2 virus 3' ITR, respectively;

(b) the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially mirror images of each other;

(c) the 5' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:36, and the 3' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:37; and/or

(d) the 5' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:38, and the 3' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:39.

3. The AAV of claim 1 or claim 2, wherein the correction genome has an essential absence of a promoter operatively linked to the editing element nucleotide sequence, or the correction genome further comprises an exogenous promoter operatively linked to the editing element.

4. The AAV of any one of claims 1 to 3, wherein the replication-defective AAV genome comprises an essential absence of an AAV *rep* gene and an AAV *cap* gene.

5. The AAV of any one of claims 1 to 4, wherein:

(a) each of the 5' and 3' homologous arm nucleotide sequences independently has a nucleotide length of between about 500 to 1000 nucleotides or between about 600 to 1000 nucleotides;

(b) the 5' and 3' homologous arm nucleotide sequences have substantially equal nucleotide lengths;

(c) the 5' and 3' homologous arm nucleotide sequences have asymmetrical nucleotide lengths;

(d) the 5' homologous arm nucleotide sequence has at least about 95% nucleotide sequence identity to the 5' region of the mammalian chromosome relative to the target locus;

(e) the 3' homologous arm nucleotide sequence has at least about 95% nucleotide sequence identity to the 3' region of the mammalian chromosome relative to the target locus; and/or

(f) the 5’ homologous arm nucleotide sequence has 100% sequence identity to the 5’ region of the mammalian chromosome relative to the target locus and the 3’ homologous arm nucleotide sequence has 100% sequence identity to the 3’ region of the mammalian chromosome relative to the target locus.

6. The AAV of any one of claims 1 to 5, wherein:

(a) the editing element consists of one nucleotide, wherein the target locus is selected from a nucleotide sequence consisting of one nucleotide, and the target locus represents a point mutation of the mammalian chromosome;

(b) the editing element comprises at least 1, 2, 10, 100, 200, 500, 1000, 1500, 2000, 3000, 4000, or 5000 nucleotides;

(c) the editing element comprises 1 to 5500, 1 to 5000, 1 to 4500, 1 to 4000, 1 to 3000, 1 to 2000, 1 to 1000, 1 to 500, 1 to 200, or 1 to 100 nucleotides, or 2 to 5500, 2 to 5000, 2 to 4500, 2 to 4000, 2 to 3000, 2 to 2000, 2 to 1000, 2 to 500, 2 to 200, or 2 to 100 nucleotides, or 10 to 5500, 10 to 5000, 10 to 4500, 10 to 4000, 10 to 3000, 10 to 2000, 10 to 1000, 10 to 500, 10 to 200, or 10 to 100 nucleotides;

(d) the editing element comprises an exon, an intron, a 5’ untranslated region (UTR), a 3’ UTR, a promoter, a splice donor, a splice acceptor, a sequence encoding or non-coding RNA, an insulator, a gene, or a combination thereof, wherein the editing element is a fragment of a coding sequence of a gene selected from a fragment within the target locus and a fragment spanning the target locus;

(e) the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to one, the editing element comprises m nucleotides where m is an integer equal to n, and the editing element represents a substitution for the target locus of the mammalian chromosome;

(f) the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to one, the editing element comprises m nucleotides where m is an integer greater than n, and the editing element represents a substitutive addition for the target locus of the mammalian chromosome;

(g) the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to two, the editing element comprises m nucleotides where m is an integer less than n, and the editing element represents a substitutive deletion for the target locus of the mammalian chromosome;

(h) the target locus is an internucleotide bond, the editing element comprises m nucleotides where m is an integer greater than or equal to one, and the editing element represents an addition for the target locus of the mammalian chromosome;

(i) the editing element is an internucleotide bond, wherein the target locus comprises a nucleotide sequence comprising one or more nucleotides, and the editing element comprises a deletion for the target locus of the mammalian chromosome; and/or

(j) the target locus of the mammalian chromosome is a mutant target locus comprising one or more mutant nucleotides, relative to a corresponding wild type mammalian chromosome, wherein:

(i) the mutant target locus comprises a point mutation, a missense mutation, a nonsense mutation, an insertion of one or more nucleotides, a deletion of one or more nucleotides, or combinations thereof;

(ii) the mutant target locus comprises an amorphic mutation, a neomorphic mutation, or an antimorphic mutation;

(iii) the mutant target locus comprises an autosomal dominant mutation, an autosomal recessive mutation, a heterozygous mutation, a homozygous mutation, or combinations thereof; and/or

(iv) the mutant target locus is selected from a promoter, an enhancer, a signal sequence, an intron, an exon, a splice donor site, a splice acceptor site, an internal ribosome entry site, an inverted exon, an insulator, a gene, a chromosomal inversion, and a chromosomal translocation within the mammalian chromosome.

7. The AAV of any one of claims 1 to 6, wherein:

(a) the AAV capsid protein comprises the amino acid sequence of amino acids 203-736 of SEQ ID NO: 2, 3, 4, 6, 7, 10, 11, 12, 13, 15, 16, or 17;

(b) the AAV capsid protein comprises the amino acid sequence of amino acids 138-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, or 17;

(i) (c) the AAV capsid protein comprises an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 1-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, or 17.

8. The AAV of any one of claims 1 to 7, wherein:

(a) the mammalian chromosome is selected from human chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, X and Y;

(b) the mammalian chromosome is selected from mouse chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, X and Y;

(c) the mammalian chromosome is not human chromosome 19;

(d) the mammalian chromosome is a somatic cell chromosome, wherein:

(i) the somatic cell is from a tissue selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue and epithelial tissue;

(ii) the somatic cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage; and/or

(iii) the somatic cell is a CD34+ cell;

(e) the mammalian chromosome is a stem cell chromosome, wherein the stem cell is selected from a hematopoietic stem cell, a cord blood stem cell, a bone marrow stem cell, a fetal liver stem cell, and a peripheral blood stem cell; and/or

(f) the mammalian chromosome is a chromosome of a cell selected from the group consisting of a CD34+ Hematopoietic stem cell line (HSC), a K562 CD34+ leukemia cell line, a HepG2 human liver cell line, a peripheral blood stem cell, a cord blood stem cell, a CD34+ peripheral blood stem cell, a WI-38 human diploid fibroblast cell line, a MCF7 human breast cancer cell line, a Y79 human retinoblastoma cell line, a SCID-X1 LBL human EBV-immortalized B cell line, a primary human hepatocyte, a primary hepatic sinusoidal endothelial cell, and a primary skeletal muscle myoblast.

9. The AAV of any one of claims 1 to 8, wherein the AAV has a chromosomal integration efficiency of at least about 5% or at least about 10% for integrating the editing element into the target locus of the mammalian chromosome in the cell.

10. A composition comprising an adeno-associated virus (AAV) of any one of claims 1 to 9, wherein the composition is in a pharmaceutically acceptable formulation, wherein:

(a) the formulation is constituted for administration to a mammal;

(b) the formulation is constituted for administration to a mammal via intravenous injection, subcutaneous injection, intramuscular injection, autologous cell transfer, or allogeneic cell transfer; and/or

(c) the formulation comprises an excipient, wherein the excipient is selected from a carrier, an adjuvant, a vehicle, and combinations thereof.

11. A packaging system for recombinant preparation of an adeno-associated virus (AAV), wherein the packaging system comprises:

(a) a Rep nucleotide sequence encoding one or more AAV Rep proteins;

(b) a Cap nucleotide sequence encoding one or more AAV capsid proteins as set forth in any one of claims 1 to 9; and

(c) a correction genome as set forth in any one of claims 1 to 9;

wherein the packaging system is operative in a cell for enclosing the correction genome in the capsid to form the AAV.

12. The packaging system of claim 11, wherein:

(a) the packaging system comprises a first vector comprising the Rep nucleotide sequence and the Cap nucleotide sequence, and a second vector comprising the correction genome; and/or

(b) the Rep nucleotide sequence encodes an AAV2 Rep protein, wherein the AAV2 Rep protein comprises one or both of Rep 78/68 and Rep 68/52; and/or the AAV2 Rep protein comprises an amino acid sequence having a minimum percent sequence identity to the AAV2 Rep amino acid sequence of SEQ ID NO: 40, wherein the minimum percent sequence identity is at least 70% across the length of the amino acid sequence encoding the AAV2 Rep protein.

13. The packaging system of claim 11 or claim 12, further comprising a third vector, wherein the third vector is a helper virus vector, wherein:

(a) the helper virus vector is an independent third vector;

(b) the helper virus vector is integral with the first vector;

(c) the helper virus vector is integral with the second vector;

(d) the third vector comprises genes encoding helper virus proteins; and/or

(e) the helper virus is selected from the group consisting of adenovirus, herpes virus, vaccinia virus, and cytomegalovirus (CMV); wherein

(i) the adenovirus genome comprises one or more adenovirus RNA genes selected from the group consisting of E1, E2, E4 and VA; or

(f) the helper virus is herpes simplex virus (HSV), wherein the HSV genome comprises one or more HSV genes selected from the group consisting of UL5/8/52, ICPO, ICP4, ICP22 and UL30/UL42.

14. The packaging system of any one of claims 11 to 13, wherein:

(a) the first vector and the third vector are contained within a first transfecting plasmid;

(b) the nucleotides of the second vector and the third vector are contained within a second transfecting plasmid;

(c) the nucleotides of the first vector and the third vector are cloned into a recombinant helper virus; or

(d) the nucleotides of the second vector and the third vector are cloned into a recombinant helper virus.

15. A method for recombinant preparation of an adeno-associated virus (AAV), wherein the method comprises introducing the packaging system of any one of claims 11 to 14 into a cell under conditions operative for enclosing the correction genome in the capsid to form the AAV.

16. An *ex vivo* method for editing a target locus of a mammalian genome, wherein the method comprises transducing a mammalian cell comprising the mammalian genome with an adeno-associated virus (AAV) of any one of claims 1 to 9, wherein:

(a) the mammalian cell is from a tissue selected from the group consisting of connective tissue comprising blood, muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue;

(b) the mammalian cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage;

(c) the mammalian cell is a stem cell, wherein the stem cell comprises one or more stem cells selected from the group consisting of a hematopoietic stem cell, a cord blood stem cell and a peripheral blood stem cell; or

(d) the mammalian cell is one or more of the group consisting of a myoblast, an endothelial cell, a liver cell, a fibroblast, a breast cell, a lymphocyte, and a retinal cell.

17. The method of claim 16, wherein:

(a) the AAV is transduced without co-transducing an exogenous nuclease or a nucleotide sequence that encodes an exogenous nuclease;

(b) the AAV has a chromosomal integration efficiency of at least about 1%, 2%, 3%, 4% or 5% for integrating the editing element into the target locus of the mammalian chromosome;

(c) the editing element of the correction genome is integrated into the target locus of the mammalian chromosome with a chromosomal integration efficiency of at least 10%, 20%, 40%, or 50% of the mammalian cells;

(d) the editing element of the correction genome is integrated into the target locus of the mammalian chromosome with a chromosomal integration efficiency ranging from 10% to 70%, 20% to 70%, 40% to 70%, or 50% to 70% of the mammalian cells;

(e) the AAV has a chromosomal integration efficiency further characterized by an allele frequency in a population of cells of at least about 10%, at least about 50%, or at least about 75% for the allele comprising the editing element integrated into the target locus of the mammalian chromosome; and/or

(f) the allele frequency in a population of cells is an allele frequency in a population of cells in vitro.

18. A method for generating a transgenic non-human animal, the method comprising:

transducing a non-human animal cell with the AAV of any one of claims 1 to 9 or the composition of claim 10 and implanting the cell into a host non-human animal under conditions sufficient to generate a transgenic non-human animal from the host non-human animal, wherein:

(i) the non-human animal cell is derived from a zygote or an embryo of a non-human animal; and/or

(ii) the non-human animal cell is derived from a zygote or an embryo of a non-human animal.

19. A transgenic non-human animal obtained by the method of claim 18.

20. A tissue derived from the transgenic non-human animal of claim 19.

21. The tissue of claim 20, wherein:

(a) the tissue is selected from the group consisting of connective tissue comprising blood, muscle tissue, nervous tissue, endothelial tissue and epithelial tissue; or

(b) the tissue is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

22. A cell derived from the transgenic non-human animal of claim 19.

23. The cell of claim 22, wherein:

(a) the cell is a primary cell;

(b) the cell is a CD34+ cell, a hepatocyte, a myoblast, an endothelial cell, a liver cell, a fibroblast, a breast cell, a lymphocyte, or a retinal cell;

(c) the cell is an inducible pluripotent stem (iPS) cell;

(d) the cell is from a tissue selected from the group consisting of connective tissue comprising blood, muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue;

(e) the cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage; and/or

(f) the cell is a stem cell, wherein the stem cell is selected from the group consisting of a hematopoietic stem cell, a cord blood stem cell, and a peripheral blood stem cell.

24. A cell obtained by the method of claim 16.

25. The AAV of any one of claims 1 to 9, or the composition of claim 10, for use as a medicament.